REMARKS

Favorable reconsideration of the subject application as amended above is respectfully requested in view of the comments below.

Claims 13-26 are pending in the present application. Claims 16 and 18-22 have been withdrawn from consideration. Claim17 is canceled herein and rewritten in independent format as new claim 27. Accordingly, claims 13-15, 17,and 18-27 are presented for examination on the merits.

Claims 13 has been amended to more particularly define the radiation treatment as ionizing radiation treatment. This amendment is supported by the disclosure at paragraph 11 where it is disclosed that the radiation is for prostate cancer, which is known in the art to be ionizing radiation. Accordingly, no new matter is added by this amendment to the claims. Further, this amendment does not require further searching because the term "ionizing radiation" is much narrower than the term "radiation" that was used by the Examiner in searching the prior art. Thus, it is respectfully requested that the claim amendments be entered.

Applicants and their attorney would like to thank the Examiner for graciously allowing an interview to discuss the outstanding Office Action. The Examiner's comments and suggestions are appreciated and the amendments above are made in the spirit of compliance with the Examiner's suggestions.

Claims 13-15, 17 and 23-16 are rejected under 35 U.S.C. § 103(a) over Collins *et al.* in view of Kutilek, Wilder, Bull and Shafron. The Examiner relies on Collins as teaching use of COX2 inhibitors to treat acute and chronic inflammatory diseases including chromic fatigue syndrome or side effects from radiation therapy. The Examiner relies on Kutilek as teaching that

fatigue is a common side effect of radiation therapy; Bull as teaching that fatigue, chills and fever are symptoms of inflammation which can be treated by treating the inflammation; Wilder is relied on as teaching use of COX2 inhibitors to treat the side effects of sunburn, which include fatigue; and Shafron is relied on as teaching the use of COX2 inhibitors to treat the side effects associated with use of rifabutin and macrolide in the treatment of Crohn's disease. The Examiner also states that it is common knowledge that fatigue is mediated by an inflammatory process. The Examiner concludes, therefore, that it would have been obvious to use a COX2 inhibitor to reduce fatigue associated with radiation therapy.

This rejection is respectfully traversed as follows.

The present invention is directed to a method for reducing or eliminating fatigue as a side effect of ionizing radiation therapy. Such radiation therapy is commonly provided to cancer patients and is known to cause fatigue in a significant portion of the treated population. The inventors have discovered that the administration of COX2 inhibitors significantly decreases or eliminates fatigue associated with ionizing radiation therapy.

As discussed during the interview and in great detail in the Response to Office Action filed January 29, 2004, the source of the fatigue that is commonly associated with ionizing radiation treatment is currently not known. *See* Jaconsen and Thors, and Geinitz *et al.* (of record). As these references discuss in detail, there are many hypothesis concerning the source of fatigue during radiation therapy, but the cause remains unknown. However, Geinitz *et al.* specifically dismiss elevated cytokines as the possible source of fatigue (p. 694, right column).

Thus, the Examiner's reliance on the primary reference, which teaches that chronic fatigue and some side effects of radiation therapy are caused by elevated IL-1 levels has no relevance to the examination of the present application. Collins does not disclose or suggest that fatigue

associated with ionizing radiation treatment is an IL-1 mediated condition, nor does this reference identify any side effect of ionizing radiation therapy that is caused by elevated IL-1 levels. Thus, in view of the teachings of Geinitz *et al.* one of ordinary skill in the art would not rely on the teachings of Collins *et al.* as suggested by the Examiner since this reference is strictly limited to treatment for IL-1 mediated diseases, *e.g.*, chronic fatigue, arthritis, etc. and Geinitz specifically teaches that elevated cytokine levels **are not responsible** for fatigue associated with ionizing radiation therapy.

The secondary references relied on by the Examiner do not compensate for the shortcomings of the primary reference. Wilder is not relevant to the examination of the present application, since this reference is directed to treatments for the side effects of non-ionizing radiation. Kutilek merely teaches that it is known in the art that ionizing radiation therapy is often associated with fatigue; and Shafron is directed to methods for reducing the side effects of antibiotic treatment for Crohn's disease; and Bull is directed to methods for determining the degree of systemic inflammation in an individual.. None of these references teaches or suggests anything about fatigue associated with ionizing radiation therapy. In particular, none of these references discloses or suggests that the fatigue associated with ionizing radiation therapy is an inflammatory response. As such, the combined art fails to render the claimed invention obvious.

It is therefore submitted that the claims are clearly patentable over all the prior art of which Applicant is aware and are believed to be in condition for allowance. Accordingly, such action is respectfully solicited.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 500417 and please credit any excess fees to such deposit account.

Respectfully submitted,

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Date: August 18, 2004